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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/662,431	09/16/2003	Steven M. Ruben	9593-036	2661

20583 7590 09/22/2004

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EXAMINER	
HUYNH, PHUONG N	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/662,431	RUBEN, STEVEN M.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/1/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-41 pending.

2. Applicant's election with traverse of Group I Claims 1-41 drawn to an isolated antibody that specifically binds to the AIM-I comprising SEQ ID NO: 2, a hybridoma cell line producing said antibody, a composition and kit comprising said antibody, filed 7/1/04, is acknowledged. The traversal is on the grounds that Groups 1 and 2 are directed to anti-AIM-I antibodies, hybridoma cell lines, compositions and kits. Specifically, Group 1 relates to an isolated antibody that specifically binds to AIM-l, a hybridoma cell line producing said antibody, a composition and kit comprising said antibody, and Group 2 relates to a kit comprising a nucleic acid probe capable of hybridizing to AIM-I RNA, or a pair of nucleic acid primers capable of priming, amplification of at least a portion of an AIM-I nucleic acid. Applicant submits that a search of the art relevant to one group, Group 1, would necessarily overlap and identify art relevant to the other group, Group 2. Accordingly, Applicant submits that to search the subject matter to Groups 1 and 2 together would not be a serious burden on the Examiner. Even assuming arguendo that the two groups were to be considered distinct inventions, Applicant asserts that, pursuant to MPEP § 803, the subject matter of claims 1-41 can be examiner together in a single application without imposing a serious burden to the Examiner. Applicant respectfully points out that the subject matter of Groups 1 and 2 are in the same class and subclass, Class 435, subclass 810. Thus, in view of MPEP § 803, Groups 1 and 2 should be examiner together, since such examination would not be a "serious burden" on the Examiner.

This is not found persuasive because of the reasons set forth in the restriction mailed 5/3/04. As is well known in the art, nucleic acid probe and primer binds to or capable of hybridizes to AIM-I RNA whereas antibodies are proteins that bind to other proteins. The two types of molecules therefore have different functions - the hybridizing nucleic acid versus binding to other protein, different modes of operation – DNA-RNA interactions versus protein-protein interactions - and different effects – interacting with nucleic acids versus interacting with another protein. Thus, as was stated in the previous office action, they differ structurally and functionally and cannot be used together or interchangeably, Reasons as to why the other groups are distinct are also provided in the previous office action. Further, a prior art search also requires a literature search. It is a burden to search more than one invention. With respect to the argument

that the search and examination of all groups would not entail a "serious burden", the separate classification such as Class 530 and Class 424 for antibodies and Class 536 for nucleic acid probe of the different groups provides prima facie evidence of such a burden; see MPEP § 803. Furthermore, antibodies, and nucleic acid probe represent different inventions and require different, non-contiguous searches, as evidenced by their different classification. They require separate searches of separate databases. A search of polynucleotide databases does not reveal information about protein sequences or the antibody, nor does a search of antibody or polypeptide databases reveal information about polynucleotides. Thus to consider all of these groups would constitute an undue burden because each requires considerations that are separate from each of the others. Therefore, the requirement of Group 1 and Group 2 is still deemed proper and is therefore made FINAL.

3. Claims 1-41, drawn to an isolated antibody that specifically binds to the AIM-I comprising SEQ ID NO: 2, a hybridoma cell line producing said antibody, a composition and kit comprising said antibody, are being acted upon in this Office Action.

4. Claim 41 is objected to because the claim encompasses non-elected embodiments.

5. The disclosure is objected to for failing to comply with the requirement of 37 C.F.R. 1.821(d), SEQ ID NO is required for page 47, paragraphs 0211 and 0212, Appropriate correction is required.

6. The disclosure is objected to because of the following informality: "die" on page 15, line 5 should have been "the". Appropriate action is required.

7. Applicant is reminded that declaration, such as those under 37 C.F.R. § 1.131 and 37 C.F.R. § 1.132, filed during prosecution of the parent application 08/816,981 do not automatically become a part of this application. Where it is desired to rely on an earlier filed affidavit, the applicant should make the remarks of record in the later application and include a copy of the original affidavit filed in the parent application.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 22-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the plasmid containing the human cDNA with ATCC Deposit No. 97448 is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification.

If the deposit has been made under the terms of the Budapest Treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the plasmid containing the human cDNA with ATCC Deposit No. 97448 have been deposited under the Budapest Treaty and that the plasmid containing the human cDNA with ATCC Deposit No. 97448 will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample or **for the enforceable life of the patent whichever is longer**. See 37 CFR 1.806.

If the deposit has not been made under the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature must be made, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been met.

10. Claims 13-19, and 21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for an isolated antibody that specifically binds the Apoptosis Inducing Molecule (AIM-I) protein comprising SEQ ID NO: 2 or an isolated antibody that specifically binds the Apoptosis Inducing Molecule (AIM-I) protein consisting of SEQ ID NO: 2, **does not** reasonably provide enablement for any isolated antibody (claim 13) such as monoclonal (claim 14), polyclonal, chimeric, humanized and human antibody (claim 21) and antigen binding

fragment thereof (claim 17) that specifically binds an Apoptosis Inducing Molecule (AIM-I) polypeptide wherein said polypeptide "comprises" an amino acids 39 to 281 of SEQ ID NO: 2 wherein said antibody is an antagonist of AIM-1 (Claim 15), which blocks binding of AIM-I to any target cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only an isolated antibody such as monoclonal, polyclonal, humanized, or chimeric antibody that specifically binds to the full length Apoptosis Inducing Molecule (AIM-I) protein comprising SEQ ID NO: 2 or an isolated antibody that specifically binds the Apoptosis Inducing Molecule (AIM-I) protein consisting of SEQ ID NO: 2 or the polypeptide encoded by the human cDNA contained in ATCC Deposit No. 97448.

The specification does not teach how to make any antibody that binds to *all* polypeptide comprises amino acids 39 to 281 of SEQ ID NO: 2 because the term "comprising" is open-ended. It expands that polypeptide to include additional amino acids at either or both ends. There is insufficient guidance as to which undisclosed amino acids to be added and whether the resulting antibody such as polyclonal, monoclonal, chimeric, humanized, or human antibody still binds specifically to the polypeptide comprising SEQ ID NO: 2, much less about the claimed antibody is antagonist to protein of SEQ ID NO: 2. Given the indefinite number of polypeptide "comprises" amino acids 39 to 281 of SEQ ID NO: 2, there is a lack of working example demonstrating all antibody binds specifically to the polypeptide comprising SEQ ID NO: 2, let alone the antibody is antagonist to the protein of SEQ ID NO: 2.

Stryer *et al* teach that a protein is highly dependent on the overall structure of the protein itself and that the primary amino acid sequence determines the conformational of the protein (See enclosed appropriate pages).

Ngo *et al* teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (See Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

Kuby *et al*, teach that antibody epitopes (B cell epitopes) are not linear and are comprised of complex three-dimensional array of scattered residues which will fold into specific conformation that contribute to binding (See Kuby 1994, page 94, in particular). Immunization with a peptide fragment derived from a full-length polypeptide may result in **antibody specificity** that differs from the antibody specificity directed against the native full-length polypeptide. Without the specific amino acid residues, it is unpredictable which antibody would bind specifically to a polypeptide "comprises" amino acids 39 to 281 of SEQ ID NO: 2.

Abaza *et al*, teach that even a single amino acid substitution outside the antigenic site can exert drastic effects on the reactivity of a protein with monoclonal antibody against the site (See abstract, in particular).

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

11. Claims 13-19, and 21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of all isolated antibody (claim 13) such as monoclonal (claim 14), polyclonal, chimeric, humanized and human antibody (claim 21) and antigen binding fragment thereof (claim 17) that specifically binds an Apoptosis Inducing Molecule (AIM-I) polypeptide wherein said polypeptide "comprises" an

amino acids 39 to 281 of SEQ ID NO: 2 wherein said antibody is an antagonist of AIM-1 (Claim 15), which blocks binding of AIM-I to any target cell.

The specification discloses only an isolated antibody such as monoclonal, polyclonal, humanized, or chimeric antibody that specifically binds to the full length Apoptosis Inducing Molecule (AIM-I) protein comprising SEQ ID NO: 2 or an isolated antibody that specifically binds the Apoptosis Inducing Molecule (AIM-I) protein consisting of SEQ ID NO: 2 or the polypeptide encoded by the human cDNA contained in ATCC Deposit No. 97448.

With the exception of the specific antibody that binds to the specific polypeptide mentioned above, there is insufficient written description about the structure associated with function of all polypeptide "comprises" amino acids 39 to 281 of SEQ ID NO: 2 to which the claimed antibody binds without the amino acid sequence. The term "comprises" is open-ended. It expands the polypeptide to include additional amino acids at either or both ends of SEQ ID NO: 2. There is inadequate written description about which undisclosed amino acids to be added and whether the resulting antibody such as monoclonal, polyclonal, humanized, chimeric, human antibody and binding fragment thereof still bind specifically to polypeptide of SEQ ID NO: 2.

Given the lack of a written description about the polypeptide "comprises" amino acids 39 to 281 of SEQ ID NO: 2 to which the claimed antibody binds, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species of polypeptide to describe the genus for the claimed antibody that specifically binds to all polypeptide comprises amino acids 39 to 281 of SEQ ID NO: 2. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398; University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC2004).*

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

13. Claims 1-12, 26-30 and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The "of SEQ ID NO: 2" in claims 1, 26, and 29 is ambiguous and indefinite because it is not clear if claimed isolated antibody specifically binds to the Apoptosis Inducing Molecule (AIM-I) is comprising or consisting of SEQ ID NO: 2. If it is intended to be open-ended, it is suggested that "comprising" be used. If is intended to be close, it is suggested that "consisting of" be recited in claim 1.

The "anti-AIM-I antibody" in claim 41 is indefinite because "AIM-I" is merely a laboratory designation which does not clearly define the claimed product, since different laboratories may use the same laboratory designation to define completely distinct antibody. It is suggested that the claim be amended to recite "A kit comprising in one or more containers an isolated antibody that specifically binds to the Apoptosis Inducing Molecule (AIM-I) protein comprising SEQ ID NO: 2".

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

15. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

16. Claims 1-40 are rejected under 35 U.S.C. 102(e) as being anticipated by US Pat No. 6,521,228 B1 (filed June 29, 1995; PTO 1449).

The '228 patent teaches various isolated antibodies such as polyclonal, monoclonal, chimeric, humanized, and binding fragment thereof such as Fab, F(ab'), and (F(ab')2 that bind to a polypeptide known as TRAIL which is 100% identical to the claimed Apoptosis Inducing Molecule (AIM-I) (See col. 30, lines 8 bridging col. 31, lines 65, Example 4, col. 30, lines 16-20, claims 1-35 of '228, reference SEQ ID NO: 2, in particular). The reference antibody blocks the binding of the reference polypeptide to a target cell (See col. 31, lines 36-41, in particular). The '288 patent further teaches a hybridoma cell line that produces the reference monoclonal antibody (See col. 34, line 63 bridging col. 35, lines 1-6, claims 8, 31-32 and 35 of '228, in particular). The '228 patent teaches a composition comprising the reference antibody and a pharmaceutically acceptable carrier (See col. 31, lines 65 bridging col. 32, line 1, claims 9-10 of '228, in particular). Claims 13-19 and 21 are included in this rejection because the term "comprising" is open-ended. It expands the polypeptide to which the claimed antibody and fragment thereof bind to include additional amino acids at either or both ends to include the reference polypeptide. The reference polypeptide SEQ ID NO: 2 is purified from a cell culture wherein the reference cells in said cell culture comprise a polynucleotide encoding the reference polypeptide of SEQ ID NO: 2 (See col. 37, production of Soluble TRAIL polypeptide, in particular). Claim 22-25 are included in this rejection because the binding specificity of the claimed antibody such as monoclonal, polyclonal, chimeric, humanized antibody that binds to SEQ ID NO: 2 encoded by the cDNA contained in ATCC Deposit No. 97448 appears to be the same as that of the antibody such as monoclonal, polyclonal, chimeric, humanized antibody that binds to SEQ ID NO: 2 of the prior art. Since the Patent Office does not have the facilities for examining and comparing the antibodies of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977). Thus, the reference teachings anticipate the claimed invention.

17. Claims 1-41 are rejected under 35 U.S.C. 102(e) as being anticipated by 6,030,945 (filed Jan 9, 1996; PTO 1449).

The '945 patent teaches various isolated antibodies such as polyclonal (col. 22, lines 50, I particular), monoclonal (see col. 23, lines 8, in particular), chimeric or humanized (col. 25, line 6-55, I particular), and binding fragment thereof such as Fab fragments (see col. 24, lines 61

bridging col. 25, lines 1-5, in particular) that bind to a polypeptide known as Apo-2 Ligand which is 100% identical to the claimed Apoptosis Inducing Molecule (AIM-I) (See reference SEQ ID NO: 1, in particular). The reference antibody inherently blocks binding of the reference polypeptide to a target cell. The '945 patent further teaches a hybridoma cell line that produces the reference monoclonal antibody (See col. 23, lines 27-55, in particular). The '945 patent teaches a composition comprising the reference antibody and a pharmaceutically acceptable carrier such as buffers diluents and kit comprising the reference antibody (See col. 28, lines 22-44, in particular). Claims 13-19 and 21 are included in this rejection because the term "comprising" is open-ended. It expands the polypeptide to which the claimed antibody and fragment thereof bind to include additional amino acids at either or both ends to include the reference polypeptide. The reference polypeptide SEQ ID NO: 2 is purified from a cell culture wherein the reference cells in said cell culture comprise a polynucleotide encoding the reference polypeptide of SEQ ID NO: 2 (See col. 33, Purification of recombinant human Apo-2 ligand, in particular). Claim 22-25 are included in this rejection because the binding specificity of the claimed antibody such as monoclonal, polyclonal, chimeric, humanized antibody that binds to SEQ ID NO: 2 encoded by the cDNA contained in ATCC Deposit No. 97448 appears to be the same as that of the antibody such as monoclonal, polyclonal, chimeric, humanized antibody that binds to SEQ ID NO: 2 of the prior art. Since the Patent Office does not have the facilities for examining and comparing the antibodies of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977). Thus, the reference teachings anticipate the claimed invention.

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

19. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

20. Claim 41 is rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 6,521,228 B1 (filed June 29, 1995; PTO 1449) in view of US Pat No 6,030,945 (filed Jan 9, 1996; PTO 1449).

The teachings of the '228 patent have been discussed supra.

The invention in claim 41 differs from the teachings of the reference only in that a kit comprising in one or more containers a molecule consisting of an anti-AIM-I antibody.

The '945 patent teaches a kit comprising in one or more containers a molecule consisting of the antibody that binds specifically to the reference polypeptide known as Apo-2 Ligand which is 100% identical to the claimed Apoptosis Inducing Molecule (AIM-I) for therapeutic and non-therapeutic applications (See reference SEQ ID NO: 1, col. 28, lines 22-44, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the antibody as taught by the '945 patent for the antagonist antibody as taught by the '228 patent for therapeutic and non-therapeutic applications as taught by the '945 patent. One would have been motivated, with a reasonable expectation of success, to place the antibody taught by the '228 patent in a kit as taught by the '945 patent for convenience and commercial expedience. A kit will allow for ease of use for the practitioner since all the necessary reagents, standard and instructions for use are included in a kit as taught by '945 patent (See column 28, lines 40-44, in particular). From the teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidence by the references.

21. Claims 1-5, 8-11, 13-16, 18-25, 29-31, 35 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wiley *et al* (Immunity 3: 673-682, Dec 1995; PTO 1449) in view of Campbell *et al* (in Monoclonal Antibody Technology, 1984, Elsevier Science Publisher, New York, NY, page 1-32; PTO 1449).

Wiley *et al* teach a purified protein designated TNF-related apoptosis-inducing ligand (TRAIL) comprising a polypeptide sequence of that is that is 100% identical to the claimed amino acids 1 to 281 of SEQ ID NO: 2 (Fig. 1, in particular) wherein the reference protein induces apoptosis in various cell lines derived from pathological leukemia such as Bjab, Ramos, 17937 or T cell such as Jurkat cell (See Table 1 on page 678, Fig 3, lane 4, in particular). Wiley et al teach a purified soluble protein which is a fragment of TRAIL comprising the extra cellular domain (amino acids 95-281) of the reference polypeptide (See Fig 7 on page 679, page 675, column 1, in particular) wherein the reference protein induces apoptosis in various cell lines derived from pathological leukemia such as Bjab, Ramos, U937 or T cell such as Jurkat cell (See Table 1 on page 678, Fig 3, lane 4, in particular).

The invention in claim 1 differs from the teachings of the reference only in that an antibody that specifically binds the Apoptosis Inducing Molecule (AIM-I) protein of SEQ ID NO: 2.

The invention in claims 2 and 23 differs from the teachings of the reference only in that the antibody is a monoclonal antibody that specifically binds the Apoptosis Inducing Molecule (AIM-I) protein of SEQ ID NO: 2.

The invention in claim 3 differs from the teachings of the reference only in that the antibody that specifically binds the Apoptosis Inducing Molecule (AIM-I) protein of SEQ ID NO: 2 is an antagonist of the protein of SEQ ID NO: 2.

The invention in claim 4 differs from the teachings of the reference only in that an antibody that specifically binds the Apoptosis Inducing Molecule (AIM-I) protein of SEQ ID NO: 2 which blocks binding of AIM-1 to a target cells.

The invention in claim 5 differs from the teachings of the reference only in that an antibody that specifically binds the Apoptosis Inducing Molecule (AIM-I) protein of SEQ ID NO: 2 which blocks binding of AIM-1 to a target cells wherein the antibody is a monoclonal antibody.

The invention in claims 8, 18 differs from the teachings of the reference only in that a hybridoma cell line that produces the monoclonal antibody that specifically binds the Apoptosis Inducing Molecule (AIM-I) protein of SEQ ID NO: 2.

The invention in claim 9 differs from the teachings of the reference only in that a composition comprising the antibody that specifically binds the Apoptosis Inducing Molecule (AIM-I) protein of SEQ ID NO: 2 and a pharmaceutically acceptable carrier.

The invention in claim 10 differs from the teachings of the reference only in that a composition comprising the monoclonal antibody that specifically binds the Apoptosis Inducing Molecule (AIM-I) protein of SEQ ID NO: 2 and a pharmaceutically acceptable carrier.

The invention in claim 11 differs from the teachings of the reference only in that the antibody that specifically binds the Apoptosis Inducing Molecule (AIM-I) protein of SEQ ID NO: 2 is an antagonist of the protein of SEQ ID NO: 2 wherein the antibody is a monoclonal antibody.

The invention in claim 13 differs from the teachings of the reference only in that an isolated antibody that specifically binds the Apoptosis Inducing Molecule (AIM-I) protein wherein the polypeptide comprises amino acids 39 to 281 of SEQ ID NO: 2.

The invention in claim 14 differs from the teachings of the reference only in that an isolated antibody that specifically binds the Apoptosis Inducing Molecule (AIM-I) protein wherein the polypeptide comprises amino acids 39 to 281 of SEQ ID NO: 2 wherein the antibody is a monoclonal antibody.

The invention in claims 15 and 16 differs from the teachings of the reference only in that an isolated antibody that specifically binds the Apoptosis Inducing Molecule (AIM-I) protein wherein the polypeptide comprises amino acids 39 to 281 of SEQ ID NO: 2 wherein the antibody is an antagonist of AIM-I which blocks binding of AIM-I to a target cell.

The invention in claim 19 differs from the teachings of the reference only in that an isolated antibody that specifically binds the Apoptosis Inducing Molecule (AIM-I) protein wherein the polypeptide comprises amino acids 39 to 281 of SEQ ID NO: 2 wherein the antibody is a monoclonal antibody.

The invention in claim 20 differs from the teachings of the reference only in that an antibody that specifically binds the Apoptosis Inducing Molecule (AIM-I) protein of SEQ ID NO: 2 wherein the antibody is a polyclonal antibody.

The invention in claim 21 differs from the teachings of the reference only in that an isolated antibody that specifically binds the Apoptosis Inducing Molecule (AIM-I) protein wherein the polypeptide comprises amino acids 39 to 281 of SEQ ID NO: 2 wherein the antibody is a polyclonal antibody.

Campbell *et al* teach that "it is customary now for any group working on a macromolecule to both clone the gene encoding for it and make monoclonal antibodies to it (sometimes without a clear objective for their application)" (See page 29, section Basic Research, in particular). Campbell *et al* further teach conventional antiserum which is polyclonal antibody (See page 4, comparison of monoclonal antibodies and conventional antiserum, in particular).

Therefore, it would be been obvious to one having ordinary skill in the art at the time the invention was made to produce polyclonal or monoclonal antibody that is specific for the polypeptide of SEQ ID NO: 2. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art at the time the invention was made would have been motivated with a reasonable expectation of success to generate polyclonal or monoclonal antibodies to the claimed polypeptides based on the fact that it is a conventional practice in the art to do so for further study, characterization and identification of a polypeptide as taught by Campbell *et al* since the antibody to the polypeptide of other members of the same family has an antagonistic effect on cell death as taught by Wiley *et al*. Claims 8 and 18 are include in this rejection because monoclonal antibody as taught by Campbell et al is produced by hybridoma.

Claim 22-25, 29-31, 35 and 37 are included in this rejection because the binding specificity of the claimed antibody such as monoclonal, polyclonal, chimeric, humanized antibody that binds to SEQ ID NO: 2 encoded by the cDNA contained in ATCC Deposit No. 97448 appears to be the same as that of the antibody such as monoclonal, polyclonal, chimeric, humanized antibody that binds to SEQ ID NO: 2 of the prior art. Since the Patent Office does not have the facilities for examining and comparing the antibodies of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977).

22. Claims 6-7, 12, 17, 26-28, 32-34, 36, and 38-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wiley *et al* (Immunity 3: 673-682, Dec 1995; PTO 1449) in view of Campbell *et al* (in Monoclonal Antibody Technology, 1984, Elsevier Science Publisher, New York, NY, page 1-32; PTO 1449) as applied to claims 1-5, 8-11, 13-16, 18-25, 29-31, 35 and 37 mentioned above and further in view of Harlow *et al* (in Antibodies a Laboratory Manual, 1988, Cold Spring harbor laboratory publication, Cold Spring Harbor, NY, pages 626-629, PTO 1449).

The combined teachings of Wiley *et al* and Campbell *et al* have been discussed supra.

The claimed invention in claims 6-7, 12, 17, 26-28, 32-34, 36, and 38-40 only in that the antibody that specifically binds the Apoptosis Inducing Molecule (AIM-I) protein of SEQ ID NO: 2 is an antibody fragment.

Harlow *et al* further teach a method of producing antibody fragment wherein the fragment is Fab or F(ab')2 fragment (See page 626-629, in particular). Harlow *et al* further teach that the problems of using multivalent antibodies on mammalian cells often will lead to capping and internalization of the antigen which can be overcome by using fragments of antibodies (See page 626 in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to produce antibody fragment as taught by Harlow *et al* with the antibody as taught by Willey *et al* that binds specifically to SEQ ID NO: 2 as taught by Willey *et al.* From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to make antibody and antibody fragment because Harlow *et al* teach that fragments of antibodies can overcome the problem of capping and internalization of the antigen on mammalian cell when using multivalent antibodies (See page 626 in particular).

23. Claims 1, 13, 20-21, 22, 24, and 29-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wiley *et al* (Immunity 3: 673-682, Dec 1995; PTO 1449) in view of in view of US Pat No. 6,180,370B, filed June 1995; PTO 1449).

The teachings of Wiley *et al* have been discussed supra.

The claimed invention in claim 20-21, 24, and 30 differs from the reference only by the recitation of said antibody is chimeric antibody, a humanized antibody or a human antibody.

The '370 patent teaches a method of producing chimeric antibodies (See column 55 lines 25-59; column 59, lines 65, in particular) and humanized antibodies (See column 44 line 33; column 68 lines 8-44, in particular). The '370 patent further teaches that humanized immunoglobulins (antibodies) specifically reactive with strong affinity to a predetermined antigen and remain nonimmunogenic in humans and yet be easily and economically produced in a manner suitable for therapeutic formulation and other uses (See column 2, lines 29-34, in particular).

Therefore, it would be been obvious to one having ordinary skill in the art at the time the invention was made to produce humanized or chimeric antibody that is specific for the polypeptide of SEQ ID NO: 2 as taught by the '370 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art at the time the invention was made would have been motivated with an expectation of success to produce chimeric or humanized antibodies because the '370 patent teaches that chimeric antibody has proven somewhat successful since chimeric antibody can loose the affinity for the antigen; humanized immunoglobulin (antibody) binds with strong affinity to a predetermined antigen and remain nonimmunogenic in humans and yet be easily and economically produced in a manner suitable for therapeutic formulation and other uses (See column 2, lines 29-34, in particular). Wiley *et al* teach that antibody to the polypeptide of other members of the same family has an antagonistic effect on cell death (See Fig 3, in particular).

24. Claims 26, 27, 32-33, 35-36, and 38-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wiley *et al* (Immunity 3: 673-682, Dec 1995; PTO 1449) in view of US Pat No. 6,180,370B, filed June 1995; PTO 1449) as applied to claims 1, 13, 20-21, 22, 24, and 29-30 mentioned above and further in view of Harlow *et al* (in Antibodies a Laboratory Manual, 1988, Cold Spring harbor laboratory publication, Cold Spring Harbor, NY, pages 626-629; PTO 1449).

The combined teachings of Wiley *et al* and '370 patent have been discussed supra.

The claimed invention in claims 27, 33, 36, and 39 only in that the antibody that specifically binds the Apoptosis Inducing Molecule (AIM-I) protein of SEQ ID NO: 2 is a humanized antibody fragment, or a human antibody fragment.

Harlow et al teach a method of producing antibodies fragment (See page 626-629, in particular). Harlow *et al* further teach that the problems of using multivalent antibodies on mammalian cells often will lead to capping and internalization of the antigen which can be overcome by using fragments of antibodies (See page 626 in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to produce antibody fragment as taught by Harlow *et al* with the humanized antibody or chimeric antibody that binds to polypeptide of SEQ ID NO: 2 as taught by the '370 patent and Wiley *et al*. From the combined teachings of the references, it is apparent that one of

ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to make antibody fragment because Harlow *et al* teach that antibody fragments such as Fab can overcome the problem of capping and internalization of the antigen on mammalian cell when using multivalent antibodies (See page 626 in particular). Wiley *et al* teach that antibody to the polypeptide of other members of the same family has an antagonistic effect on cell death (See Fig 3, in particular). The '370 patent teaches that chimeric antibody has proven somewhat successful since chimeric antibody can loose the affinity for the antigen; humanized immunoglobulin (antibody) binds with strong affinity to a predetermined antigen and remain nonimmunogenic in humans and yet be easily and economically produced in a manner suitable for therapeutic formulation and other uses (See column 2, lines 29-34, in particular).

25. Claim 41 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wiley *et al* (Immunity 3: 673-682, 1995; PTO 1449) in view of Campbell *et al* (in Monoclonal Antibody Technology, 1984, Elsevier Science Publisher, New York, NY, page 1-32; PTO 1449) as applied to claims 1-5, 8-11, 13-16, 18-25, 29-31, 35 and 37 above and further in view of U.S. Pat No. 5,858,682 (filed Aug 1996, PTO 1449).

The teachings of Wiley *et al* and Campbell *et al* have been discussed supra.

The claimed invention in claim 41 differs from the references only by the recitation of a kit comprising in one or more container consisting of anti-AIM-I antibody.

The '682 patent teaches a kit comprising an antibody for diagnostic assays (See column 3, line 40; column 6, line 17; column 8, line 36, in particular). The '682 patent further teaches an antibody which is associated with a solid phase (see column 9, line 23, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to put the monoclonal or polyclonal antibody taught by Wiley *et al* and Campbell *et al* in a kit taught by the '682 for diagnostic assays. One would have been motivated, with a reasonable expectation of success, to place the antibody taught by Wiley *et al* and Campbell *et al* in a kit for convenience and commercial expedience. A kit will allow for ease of use for the practitioner since all the necessary reagents, standard and instructions for use are included in a kit as taught by '682 (See column 8, line 36-57, in particular). From the teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable

expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidence by the references.

26. Claim 41 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wiley *et al* (Immunity 3: 673-682, 1995; PTO 1449) in view of US Pat No. 6,180,370B, (filed June 1995; PTO 1449) as applied to claims 1, 13, 20-21, 22, 24, and 29-30 above and further in view of U.S. Pat No. 5,858,682 (filed Aug 1996, PTO 1449; see entire document).

The teachings of Wiley *et al* and the '370 patent have been discussed supra.

The claimed invention in claim 41 differs from the references only by the recitation of a kit comprising in one or more container consisting of chimeric and humanized anti-AIM-I antibody.

The '682 patent teaches a kit comprising an antibody for diagnostic assays (See column 3, line 40; column 6, line 17; column 8, line 36, in particular). The '682 patent further teaches an antibody which is associated with a solid phase (see column 9, line 23, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to put the antibody taught by Wiley *et al* and the '370 patent in a kit taught by the '682 for diagnostic assays. One would have been motivated, with a reasonable expectation of success, to place the antibody taught by Wiley *et al* and the '370 patent in a kit affixed to a 96-well plate (solid phase) for convenience and commercial expedience. A kit will allow for ease of use for the practitioner since all the necessary reagents, standard and instructions for use are included in a kit as taught by '682 (See column 8, line 36-57, in particular). From the teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidence by the references.

27. No claim is allowed.

28. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message

may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (703) 872-9306.

29. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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